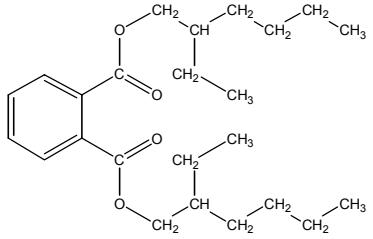
DI(2-ETHYLHEXYL) PHTHALATE
CAS No. 117-81-7
First Listed in the *Third Annual Report on Carcinogens*



CARCINOGENICITY

Di(2-ethylhexyl) phthalate [bis(2-ethylhexyl) phthalate; DEHP] is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity in experimental animals (NTP 217, 1982; IARC V.29, 1982; IARC S.7, 1987). When administered in the diet, di(2-ethylhexyl) phthalate increased the incidence of hepatocellular carcinomas in female rats, liver neoplastic nodules or hepatocellular carcinomas in male rats, and hepatocellular carcinomas in mice of both sexes.

There are no adequate data available to evaluate the carcinogenicity of di(2-ethylhexyl) phthalate in humans identified were inadequate (IARC V.29, 1982; IARC S.7, 1987).

PROPERTIES

Di(2-ethylhexyl) phthalate is a colorless, oily liquid with a slight odor. It is insoluble in water, miscible with mineral oil and hexane, and soluble in most organic solvents. Di(2-ethylhexyl) phthalate is easily dissolved in body fluids such as saliva and plasma. Di(2-ethylhexyl) phthalate is available in the United States in a variety of technical grades. Typical product specifications are the following: 99.0%-99.6% minimal ester content; 0.1% maximal moisture content; and 0.007%-0.01% acidity (as acetic acid or phthalic acid).

USE

Di(2-ethylhexyl) phthalate is used primarily as one of several plasticizers in polyvinyl chloride (PVC) resins for fabricating flexible vinyl products. According to CPSC, EPA, and FDA, these PVC resins are used to manufacture many products, including teething rings, pacifiers, soft squeeze toys, balls, vinyl upholstery, tablecloths, shower curtains, raincoats, adhesives, polymeric coatings, components of paper and paperboard, defoaming agents, enclosures for food containers, animal glue, surface lubricants, flexible devices for administering parenteral solutions, and other products that must stay flexible and noninjurious for the lifetime of their use. Di(2-ethylhexyl) phthalate also is used to manufacture vinyl gloves used for medical examinations and surgery (about 500 million pairs annually).

The only significant nonplasticizer use for di(2-ethylhexyl) phthalate is as a replacement for polychlorinated biphenyls in dielectric fluids for electric capacitors. The following miscellaneous uses for di(2-ethylhexyl) phthalate have been reported: as a solvent in erasable

ink; as an acaricide for use in orchards; as an inert ingredient in pesticides; as a component of cosmetic products; as a vacuum pump oil; in detecting leaks in respirators; and in the testing of air filtration systems. Several of these reported applications are believed to be no longer practiced or never to have been carried out on a commercial scale (IARC V.29, 1982).

PRODUCTION

The 1998 Chemical Buyers Directory identifies two domestic suppliers of di(2-ethylhexyl) phthalate (Tilton, 1997). The 1997 *Directory of Chemical Producers* indicates that there are three U.S. producers of the compound, but no amounts were disclosed (SRIa, 1997). The USITC has listed four to six manufacturers of the chemical since 1989, also without production volumes (USITC, 1990-1991, 1993-1995). In recent years, large producers have operated units used mainly for di(2-ethylhexyl) phthalate, without divulging capacities. Di(2-ethylhexyl) phthalate is the single largest volume member of the dioctyl phthalates, the common name for a group of related phthalate esters (Chem. Prod., 1989). Of total volume dioctyl phthalates production, di(2-ethylhexyl) phthalate may represent over 90%, or about 270 million lb per year (ATSDR, 1993-R047). This varies based on economics and alcohol availability.

Import and export quantities specific for di(2-ethylhexyl) phthalate were also not available. The U.S. Bureau of the Census reports imports as phthalic acid esters used as plasticizers, assumed to be predominantly dioctyl phthalates (Chem. Prod., 1989). Total U.S. dioctyl phthalate imports were 6 million lb in 1988 and 2 million lb in 1987. Imports for 1986 and 1985 were 6 and 18 million lb, respectively. Less than ten years earlier, eight companies imported only 1,500 lb in 1977. The CBI Aggregate was between 100 million and 1 billion lb (TSCA, 1979). The U.S. Bureau of the Census reports exports as dioctyl phthalates (Chem. Prod., 1989). Approximately 37 million lbs of dioctyl phthalate were exported in 1988 and 32 million lb in 1987. In 1986 and 1985, 12 and 9 million lb were exported, respectively.

Di(2-ethylhexyl) phthalate was one of the first plasticizers to be used with vinyl resins (Chem. Prod., 1989). It remains the standard of comparison. Demand for di(2-ethylhexyl) phthalate plasticized vinyl remains relatively constant. Growth in demand for flexible plastics has generally been satisfied with other plasticizers for polyvinyl chloride or other plastics such as polyolefins. Unless health concerns become greater, U.S. consumption of di(2-ethylhexyl) phthalate for the next several years will remain relatively constant. There are only limited prospects for overall growth of U.S. production of flexible polyvinyl chloride. In addition, high-performance plasticizers with specific performance properties will probably be used preferentially to dioctyl phthalate. There will also be year-to-year fluctuations since dioctyl phthalate demand usually follows the general economy. There is, however, continuing concern about the potential human carcinogenicity of di(2-ethylhexyl) phthalate. The Consumer Products Safety Commission has called for more study of di(2-ethylhexyl) phthalate. There is particular concern about the susceptibility of children to toxic effects because the plasticizer is used in pacifiers and other plastic baby products. It is also used in intravenous tubing and hemodialysis. This concern will eventually cause a reduction in di(2-ethylhexyl) phthalate use if only because of bad publicity. In the food industry, di(2-ethylhexyl) phthalate is no longer used to plasticize plastic wrap. Citric acid-based plasticizers are being evaluated to replace di(2-ethylhexyl) phthalate.

EXPOSURE

The primary routes of potential human exposure to di(2-ethylhexyl) phthalate are inhalation, ingestion, and dermal contact. A substantial fraction of the U.S. population is exposed to measurable levels of di(2-ethylhexyl) phthalate. A high-risk segment of the population consists of individuals receiving dialysis treatments or large quantities of blood that have contacted di(2-ethylhexyl) phthalate-containing tubing or containers. Among this population are hemophiliacs and dialysis patients. Estimates of exposure levels indicate that the former may be exposed to 1 to 2 mg di(2-ethylhexyl) phthalate/day and the latter to 40 mg/day. Large-volume parenteral formulations that are administered intravenously as replenishers (i.e., fluids, nutrients, electrolytes) are packaged in flexible containers made from poly(vinyl chloride) that contains phthalate as a plasticizer. The estimated concentration of di(2-ethylhexyl) phthalate in intravenous fluids is 9 to 13 ppb, while reported concentrations in whole blood and plasma stored in plastic blood bags range from 14 to 120 ppm. Another high-risk population includes workers exposed to di(2-ethylhexyl) phthalate during the formulation and processing of plastics. NIOSH estimated that about 340,000 workers were potentially exposed to di(2-ethylhexyl) phthalate in the early 1980s (ATSDR, 1993-R047). The ACGIH recommended threshold limit value (TLV) for an 8-hr time-weighted average (TWA) is 5 mg/m^3 and 10 mg/m^3 for a 15-min short-term exposure limit (STEL) (ACGIH, 1986). The National Occupational Exposure Survey (1981-1983) indicated that 147,848 workers, including 50,694 women, were potentially exposed to di(2-ethylhexyl) phthalate (NIOSH, 1984). This estimate was derived from observations of the actual use of the compound (4% of total observations) and the use of tradename products known to contain the compound (96%).

Di(2-ethylhexyl) phthalate is known to be widely distributed in the environment and has been detected in soil samples, animal and human tissues, and various forms of marine life (ATSDR, 1993-R047). The Toxic Chemical Release Inventory (EPA) listed 261 industrial facilities that produced, processed or otherwise used di(2-ethylhexyl) phthalate in 1988 (TRI, 1990). In compliance with the Community-Right-to-Know Program, the facilities reported releases of di(2-ethylhexyl) phthalate to the environment which were estimated to total 1.1 million lb. The chemical is biodegradable but tends to partition into sediment where it is relatively persistent. Disposal of plastic products containing di(2-ethylhexyl) phthalate is a major source of environmental release. Di(2-ethylhexyl) phthalate was detected in 24% of 901 surface water samples recorded in the STORET database at a medium concentration of 10 ppb. It was also found in water samples from several U.S. rivers at 0.5 to 1 ppb, and in seawater at an average concentration of 0.005 to 0.7 ppb. Another potential source of exposure is the leaching of the chemical from plastic articles in landfills (ATSDR, 1993-R047; IARC V.29, 1982).

Because of its low vapor pressure, exposure to di(2-ethylhexyl) phthalate in either water or air appears to be minimal for most individuals. It is generally accepted that low levels of phthalates occur in the atmosphere throughout the United States, with higher levels near release sources. Di(2-ethylhexyl) phthalate is a ubiquitous contaminant. For the general population, the most likely route of exposure is through contaminated food (i.e., food coming in contact with containers and wrappings containing di(2-ethylhexyl) phthalate), which provides an average intake of 0.25 mg/day and a maximum of about 2 mg/day per individual. Di(2-ethylhexyl) phthalate has been detected in such foods as milk, cheese, fish, meat, margarine, eggs, and cereal products. Most samples contained less than 1 ppm, but fatty foods contained higher levels of di(2-ethylhexyl) phthalate (ATSDR, 1993-R047).

REGULATIONS

CPSC has received the final report of an independent, nonfederal scientific panel which was convened to review the available chronic toxicity and exposure information on di(2-ethylhexyl) phthalate as used in consumer products. The Commission staff has evaluated the panel's report and agrees, in general, that di(2-ethylhexyl) phthalate should be regarded as a potential human carcinogen.

The Toy Manufacturers of America (TMA), representing pacifier and toy manufacturers, has stated that most manufacturers already have discontinued the use of di(2-ethylhexyl) phthalate in their products. The Commission staff has determined that domestic manufacturers are not using di(2-ethylhexyl) phthalate in vinyl pacifiers, and importers appear to be acquiring non-di(2-ethylhexyl) phthalate-containing pacifiers. The staff has therefore concluded that the estimated cancer risk from di(2-ethylhexyl) phthalate, which was primarily from pacifier use, has substantially declined. A TMA voluntary standard limits the amount of di(2-ethylhexyl) phthalate to less than 3% in pacifiers and teethers.

EPA regulates di(2-ethylhexyl) phthalate under the Clean Water Act (CWA), Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA), Resource Conservation and Recovery Act (RCRA), Superfund Amendments and Reauthorization Act (SARA), and Toxic Substances Control Act (TSCA). Di(2-ethylhexyl) phthalate is included on lists of chemicals for which water quality criteria have been established under CWA. A final rule reportable quantity (RQ) of 100 lb has been established for this chemical under CERCLA. Under RCRA, SARA, and TSCA, di(2-ethylhexyl) phthalate is subject to report/recordkeeping requirements. SARA sets threshold amounts for di(2-ethylhexyl) phthalate used, manufactured, or processed at a facility. Manufacturers, importers, and processors of di(2-ethylhexyl) phthalate are required to submit to EPA copies and lists of unpublished health and safety studies under TSCA. FDA regulates di(2-ethylhexyl) phthalate as an indirect food additive. NIOSH recommends an exposure limit of 5 mg/m^3 as a 10-hr time-weighted average (TWA) and a short-term exposure limit (STEL) of 10 mg/m^3. OSHA also establishes a permissible exposure limit (PEL) of 5 mg/m^3 as an 8-hr TWA and an STEL of 10 mg/m^3 for the compound. OSHA also regulates di(2-ethylhexyl) phthalate under the Hazard Communication Standard and as a chemical hazard in laboratories. Di(2-ethylhexyl) phthalate is the subject of a NIOSH Special Hazard Review because of a National Toxicology Program bioassay in which the chemical was found to be carcinogenic in rats and mice; its use in testing respirators for leaks causes additional concern. NIOSH has submitted the preliminary hazard review to OSHA. Regulations are summarized in Volume II, Table B-46.